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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/744,328	01/23/2001	Satoshi Sasaki	Q62621	4446

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EXAMINER
KAM, CHIH MIN

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 12/24/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/744,328	SASAKI ET AL.	
	Examin r	Art Unit	
	Chih-Min Kam	1653	

-- The MAILING DATE f this communication appears n the cover sheet with the c rrespondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 October 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12,17,19-22 and 25-36* is/are pending in the application.

4a) Of the above claim(s) *5,7-10,17,19-22,29 and 31-34* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6,11,12,25-28,30,35 and 36* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Claims

1. Claims 1-12, 17, 19-22 and 25-36 are pending.

Applicants' amendment filed October 15, 2002 (Paper No. 8) is acknowledged. Applicants' response has been fully considered. Claims 5, 7-10, 17, 19-22, 29 and 31-34 are non-elected invention and stand withdrawn from consideration. Claims 1, 3, 11, 12, 25, 27, 28, 35 and 36 have been amended, and claims 13-16, 18, 23 and 24 have been cancelled. Thus, claims 1-4, 6, 11, 12, 25-28, 30, 35 and 36 are examined.

Objection Withdrawn

2. The previous objection of claims 11, 12, 23, 24, 35 and 36 being improper multiple dependent claims, is withdrawn in view of applicants' cancellation of the claim, applicants' amendment to the claims, and applicants' response at page 4 in Paper No. 8.

Rejection Withdrawn

Claim Rejections - 35 USC § 101

3. The previous rejection of claims 13-16, 18, 23 and 24, under 35 U.S.C.101 regarding recitation of a use without setting forth any steps involved in the process, is withdrawn in view of applicants' cancellation of the claim.

Claim Rejections - 35 USC § 112

4. The previous rejection of claims 1, 3, 6, 11-16, 18, 23 and 24, under 35 U.S.C.112, second paragraph, regarding the claim recitation of a use without setting forth any steps involved in the process or the term "the biological activity of galectin-3", is withdrawn in view of

applicants' cancellation of the claim, applicants' amendment to the claim, and applicants' response at pages 4-5 in Paper No. 8.

Claim Rejections - 35 USC § 102

5. The previous rejection of claims 1, 2, 4, 6, 13 and 18, under 35 U.S.C. 102(b) as being anticipated by Dong *et al.* (FEBS Letters 395, 165-169 (1996)), is withdrawn in view of applicants' cancellation of the claim, applicants' amendment to the claim, and applicants' response at pages 5-6 in Paper No. 8.

Claim Objections

6. Claims 6 and 11, for example, are objected to because of the use of the term "to any of claims 1-4", the term "to any one of claims 1-4" should be used. See also claim 35.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-4, 6, 11 and 12 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification is not enabling for a pharmaceutical composition having inhibitory effect on glomerular nephritis, diabetic nephropathy or tissue fibrosis caused by the overproduction and accumulation of extracellular matrix, wherein the composition comprising a compound that promotes the production of extracellular matrix from extracellular matrix-producing cells because the specification only discloses a compound that inhibits the biological

activity of gelatin-3 also inhibits promoting the production of extracellular matrix from extracellular matrix-producing cells (page 4, line 5-21; Examples 5 and 6). The specification does not disclose a compound exhibiting the property of promoting the production of extracellular matrix from extracellular matrix-producing cells has inhibitory effect on glomerular nephritis, diabetic nephropathy or tissue fibrosis. Furthermore, there is no working example indicating such compound. Since the specification does not identify such compound nor indicates how the compound inhibits the cited disease, the one skilled in the art would not know how to make and/or use the claimed invention, thus it is necessary to have additional guidance on the identity of the compound and to carry out further experimentation to assess the effect of the compound.

The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the nature of the invention, the absence of working examples, the relative skill of those in the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

8. Claims 25-28, 30, 35 and 36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for inhibiting the overproduction and accumulation of extracellular matrix, comprising administering an identified compound that inhibits the binding of galectin-3 to the extracelluler matrix in the extracelluler matrix-producing cells, does not reasonably provide enablement for a method for inhibiting glomerular nephritis, diabetic nephropathy or tissue fibrosis caused by the overproduction and accumulation of extracellular matrix, comprising administering a compound having an inhibitory effect on the

biological activity of galectin-3 to a subject. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 25-28, 30, 35 and 36 are directed to a method for inhibiting glomerular nephritis, diabetic nephropathy or tissue fibrosis caused by the overproduction and accumulation of extracellular matrix, comprising administering a compound having an inhibitory effect on the biological activity of galectin-3 to a subject. The specification, however, only discloses cursory conclusions without data supporting the findings, which states that the compounds that inhibit the biological activity of galectin-3 can be used as a therapeutic or preventive agent for glomerular nephritis, diabetic nephropathy or tissue fibrosis which is caused by the overproduction and accumulation of extracellular matrix (page 5, lines 3-8). There are no indicia that the present application enables the full scope in view of a method for inhibiting glomerular nephritis, diabetic nephropathy or tissue fibrosis using an inhibitor of galectin-3 as discussed in the stated rejection. The present application provides no indicia and no teaching/guidance as to how the full scope of the claims is enabled. The factors considered in determining whether undue experimentation is required, are summarized in In re Wands (858 F2d at 731,737, 8 USPQ2d at 1400,1404 (Fed. Cir.1988)). The factors most relevant to this rejection are the breath of the claims, the absence of working examples, the state of the prior art and relative skill of those in the art, the unpredictability of the art, the nature of the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

(1). The breath of the claims:

The breath of the claims is broad and encompasses unspecified variants regarding the compounds that inhibit the biological activity of galectin-3, and the treating conditions for inhibiting the cited diseases, which are not adequately described or demonstrated in the specification.

(2). The absence of working examples:

There are no working examples indicating the claimed methods in association with the variants except for certain compounds such as fetuin glycoprotein and LNFP-1 which inhibit galectin-3 binding and the promotion of collagen type IV production in rat mesangium cells (Examples 5 and 6).

(3). The state of the prior art and relative skill of those in the art:

The prior art indicates galectin-3 binds to a sugar chain of glycoprotein present on the cell surface or in the extracellular matrix that activates inflammatory cells (page 1, lines 21-32 of the specification), and the overproduction and accumulation of extracellular matrix such as collagen is believed to be an important factor for the pathogenesis of the fibrosis of tissues (page 2, lines 5-13). However, the general knowledge and level of the skill in the art do not supplement the omitted description, the specification needs to provide specific guidance on the compounds inhibiting the biological activity of galectin-3 and the treating conditions for inhibiting the cited diseases to be considered enabling for the claimed method.

(4). Predictability or unpredictability of the art:

The specification has shown galectin-3 is involved in the formation of fibrosis or nephritis in rat model (Examples 1 and 2), galectin-3 has promoting effect on the collagen type IV production in mesangium cells (Example 4), and fetuin glycoprotein and LNFP-1 which

inhibit galectin-3 binding, also inhibit the promotion of collagen type IV production in rat mesangium cells (Examples 5 and 6). However, the specification does not provide the use of compounds that inhibit the biological activity of galectin-3 in inhibiting glomerular nephritis, diabetic nephropathy or tissue fibrosis, the invention is highly unpredictable regarding the effects of the compounds.

(5). The amount of direction or guidance presented and the quantity of experimentation necessary:

The claims are directed to a method for inhibiting glomerular nephritis, diabetic nephropathy or tissue fibrosis caused by the overproduction and accumulation of extracellular matrix, comprising administering a compound having an inhibitory effect on the biological activity of galectin-3 to a subject. Although galectin-3 has been shown to be involved in the formation of fibrosis or nephritis in rat model (Examples 1 and 2), and galectin-3 has promoting effect on the collagen type IV production in mesangium cells (Example 4), the specification only indicates certain compounds such as fetuin glycoprotein and LNFP-1 which inhibit galectin-3 binding also inhibit the promotion of collagen type IV production in rat mesangium cells (Examples 5 and 6). The specification has not demonstrate the use of a specific compound that inhibits the biological activity of galectin-3 in inhibiting glomerular nephritis, diabetic nephropathy or tissue fibrosis. There is no working example indicating such treatment. The specification has not provided the treating condition such as the dose, the time and the effect of a specific galectin-3 inhibitor in treating the cited diseases. Furthermore, there is no data indicating the in vitro effect can be applied to in vivo model. Since the specification fails to

provide sufficient guidance on the compound and the treating conditions used for the diseases, it is necessary to carry out further experimentation to assess the effects of these compounds.

(6). Nature of the Invention

The scope of the claims encompass using galectin-3 inhibitor for inhibiting glomerular nephritis, diabetic nephropathy or tissue fibrosis, but the specification does not provide sufficient teachings on the use of compounds in inhibiting the cited diseases. Thus, the disclosure is not enabling for the reasons discussed above.

In summary, the scope of the claim is broad, the working example does not demonstrate the claimed methods, the art is unpredictable regarding the effects of the compounds, and the guidance and the teaching in the specification are limited, therefore, it is necessary to have additional guidance and to carry out further experimentation to assess the inhibitory effect of the compound in vivo.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 1-4, 6, 11, 12, 25-28, 30, 35 and 36 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claims 1-4, 6, 11 and 12 are indefinite because of the use of the term "a compound that promotes the production of extracellular matrix from extracellular matrix-producing cells". The term of "a compound that promotes the production of extracellular matrix from extracellular

matrix-producing cells" renders the claim indefinite, it is unclear how a compound that produces an effect causing the disease would have inhibitory effect on the disease.

11. Claim 2, for example, recites the limitation " the biological activity of galectin-3" in line 2. There is insufficient antecedent basis for this limitation in claim (Note the canceled term in claim 1). See also claims 4 and 6.

12. Claims 25, 27, 30, 35 and 36 are indefinite because of the use of the term "the biological activity of galectin-3". The term of "the biological activity of galectin-3" renders the claim indefinite, it is unclear which biological activity of galectin-3 is referred to. Claims 27, 30, 35 and 36 are included in the rejection because they are dependent on a rejected claim and do not correct the deficiency of the claim from which they depend.

In response, applicants indicate independent claims 1 and 25 have been amended to include the biological activity which is to promote the production of extracellular matrix from extracellular matrix-producing cells (page 4 of the response). The argument is not found persuasive because claim 1 does not cite the biological activity of galectin-3, and claim 25 does not indicate the biological activity of galectin-3 is to promote the production of extracellular matrix from matrix-producing cells.

13. Claims 25-28, 30, 35 and 36 are indefinite because they lack essential steps as claimed in the method for inhibiting glomerular nephritis, diabetic nephropathy or tissue fibrosis in a subject. The omitted step is the outcome of the process. Claims 26-28, 30, 35 and 36 are included in the rejection because they are dependent on a rejected claim and do not correct the deficiency of the claim from which they depend.

In response, applicants indicate the effective amount of the compound used and the outcome of the treatment have been added to the claim (page 5 of the response). The argument is not found persuasive because inhibiting the overproduction and accumulation of extracellular matrix is not the endpoint of the process, the claims recites a method of inhibiting glomerular nephritis, diabetic nephropathy or tissue fibrosis in a subject, thus, the inhibition of the disease is the outcome of the process.

Conclusion

14. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (703) 308-9437. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (703) 308-2923. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-0294 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D. CMK
Patent Examiner

Christopher S. F. Low

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December 20, 2002

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